

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
21 December 2000 (21.12.2000)

PCT

(10) International Publication Number
WO 00/77037 A3

(51) International Patent Classification⁷: C12N 15/12,
C07K 14/47, 14/705, C12N 15/62, C07K 16/18, 16/28,
G01N 33/53

(21) International Application Number: PCT/US00/14042

(22) International Filing Date: 22 May 2000 (22.05.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/139,695 15 June 1999 (15.06.1999) US
60/145,070 20 July 1999 (20.07.1999) US
60/145,698 26 July 1999 (26.07.1999) US
60/149,396 17 August 1999 (17.08.1999) US
PCT/US99/20111
1 September 1999 (01.09.1999) US

PCT/US99/20594
8 September 1999 (08.09.1999) US
PCT/US99/21090
15 September 1999 (15.09.1999) US
PCT/US99/21547
15 September 1999 (15.09.1999) US
PCT/US99/28313
30 November 1999 (30.11.1999) US
PCT/US99/28301
1 December 1999 (01.12.1999) US
PCT/US99/28565
2 December 1999 (02.12.1999) US
60/169,495 7 December 1999 (07.12.1999) US
PCT/US00/00219 5 January 2000 (05.01.2000) US
PCT/US00/04341
18 February 2000 (18.02.2000) US
PCT/US00/04342
18 February 2000 (18.02.2000) US
PCT/US00/04414
22 February 2000 (22.02.2000) US

[Continued on next page]

(54) Title: SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA22779
><subunit 1 of 1, 493 aa, 1 stop
><MW: 57104, pI: 7.67, NX(S/T): 2
MRPLCVTCWMLGLLAAMGAVAGGEDGFEGTEEGSPREFIYLNRYKRAGESQDKCTYTFIVPQ
QRVTGAICVNSKEPEVLLNENRVHVKQELLELLNELLKQKRIETLQQLVEVDGGIVSEVKLLR
KESRNMNSRVTOYLMQLLHEITRKRDNALELSOLENRIINQADMLQLASKYKDLNHYQHL
ATLAHQSEIIAQLEHCQRVPSARFPVQPPPAAPPRVYQPTYNRIINQISTNEIQSDQNL
KVLPPPLTMTPTLTSLSSTDKPSGFWRDCLQALDGHDTSSIIYLVKPEENTNRLMQVWCQQR
HDPGGWTVIQRRLDGSVNFERNWETKQGFNIDGEYWLGLENIYWLTNQGNKLLVTMEDW
SGRKVFAEYASFRLEPESEYYKLRLGRYHGNAGDSFTWHNGKQFTTLDRDHDVYTGNCANHYQ
KGGWVWYACASNLNCGVYRGGHYRSRYODGVYWAEFRGGSYSLKKVVMIRPNPTFH

Important features of the protein:

Signal peptide:

amino acids 1-22

N-glycosylation sites.

amino acids 164-168, 192-196

cAMP- and GMP-dependent protein kinase phosphorylation site.

amino acids 124-128

Tyrosine kinase phosphorylation sites.

amino acids 177-184, 385-393, 385-394, 461-468

N-myristoylation sites.

amino acids 12-18, 18-24, 22-28, 29-35, 114-120, 341-347,
465-471, 473-479

Amidation site.

amino acids 373-377

Fibrinogen beta and gamma chains C-terminal domain signature.

amino acids 438-451

Fibrinogen beta and gamma chains C-terminal domain proteins.

amino acids 305-343, 365-402, 411-424, 428-458

Trehalase proteins.

amino acids 275-292

(57) Abstract: The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.



WO 00/77037 A3



PCT/US00/05601 1 March 2000 (01.03.2000) US
 PCT/US00/05841 2 March 2000 (02.03.2000) US
 PCT/US00/07377 20 March 2000 (20.03.2000) US
 PCT/US00/08439 30 March 2000 (30.03.2000) US
 PCT/US00/13358 15 May 2000 (15.05.2000) US
 PCT/US00/13705 17 May 2000 (17.05.2000) US

[US/US]; 465 Douglass Street, San Francisco, CA 94114 (US). **TUMAS, Daniel** [US/US]; 3 Rae Avenue, Orinda, CA 94563 (US). **WATANABE, Colin, K.** [US/US]; 128 Corliss Drive, Moraga, CA 94556 (US). **WILLIAMS, P., Mickey** [US/US]; 509 Alto Avenue, Half Moon Bay, CA 94019 (US). **WOOD, William, I.** [US/US]; 35 Southdown Court, Hillsborough, CA 94010 (US). **ZHANG, Zemin** [CN/US]; 876 Taurus Drive, Foster City, CA 94404 (US).

(71) **Applicant** (for all designated States except US): **GENENTECH, INC.** [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US).

(74) **Agents:** **KRESNAK, Mark, T.** et al.: Genentech, Inc., MS49, 1 DNA Way, South San Francisco, CA 94080-4990 (US).

(72) **Inventors; and**

(75) **Inventors/Applicants** (for US only): **ASHKENAZI, Avi, J.** [US/US]; 1456 Tarrytown Street, San Mateo, CA 94402 (US). **BAKER, Kevin, P.** [GB/US]; 14006 Indian Run Drive, Darnestown, MD 20878 (US). **BOTSTEIN, David** [US/US]; 2539 Somerset Drive, Belmont, CA 94002 (US). **DESNOYERS, Luc** [CA/US]; 2050 Stockton Street, San Francisco, CA 94133 (US). **EATON, Dan, L.** [US/US]; 75 Knight Drive, San Rafael, CA 94901 (US). **FERRARA, Napoleone** [US/US]; #704, 2090 Pacific Avenue, San Francisco, CA 94109 (US). **FONG, Sherman** [US/US]; 19 Basinside Way, Alameda, CA 94502 (US). **GAO, Wei-Qiang** [CN/US]; 641 Pilgrim Drive, Foster City, CA 94404 (US). **GERBER, Hanspeter** [CH/US]; #5, 1121 Tennessee Street, San Francisco, CA 94107 (US). **GERRITSEN, Mary, E.** [CA/US]; 541 Parrott Drive, San Mateo, CA 94402 (US). **GODDARD, Audrey** [CA/US]; 110 Congo Street, San Francisco, CA 94131 (US). **GODOWSKI, Paul, J.** [US/US]; 2627 Easton Drive, Burlingame, CA 94010 (US). **GURNEY, Austin, L.** [US/US]; 1 Debbie Lane, Belmont, CA 94002 (US). **KLJAVIN, Ivar, J.** [US/US]; 811 Dell Road, Pacifica, CA 94044 (US). **MATHER, Jennie, P.** [US/US]; 269 La Prenda Drive, Millbrae, CA 94030 (US). **NAPIER, Mary, A.** [US/US]; 1015 Hayne Road, Hillsborough, CA 94010 (US). **PAN, James** [CA/US]; 2705 Coronet Boulevard, Belmont, CA 94002 (US). **PAONI, Nicholas, F.** [US/US]; 1756 Terrace Drive, Belmont, CA 94002 (US). **ROY, Margaret, Ann** [US/US]; #4, 2960 Webster Street, San Francisco, CA 94123 (US). **STEWART, Timothy, A.**

(81) **Designated States (national):** AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- with (an) indication(s) in relation to deposited biological material furnished under Rule 13bis separately from the description

(88) **Date of publication of the international search report:**
 28 February 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/14042

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C07K14/705 C12N15/62 C07K16/18
C07K16/28 G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 15653 A (FERRARA NAPOLEONE ;GENENTECH INC (US); SCHWALL RALPH (US); BOTSTEI) 1 April 1999 (1999-04-01) the whole document	1-21
A	YOKOYAMA-KOBAYASHI M ET AL: "A signal sequence detection system using secreted protease activity as an indicator" GENE,NL,ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, vol. 163, no. 2, 3 October 1995 (1995-10-03), pages 193-196, XP004041983 ISSN: 0378-1119 the whole document	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

6 September 2000

Date of mailing of the international search report

22 12 2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Smalt, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/14042

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KLEIN R D ET AL: "Selection for genes encoding secreted proteins and receptors" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON, no. 93, 1 July 1996 (1996-07-01), pages 7108-7113, XP002077277 ISSN: 0027-8424 the whole document ---	
A	WO 97 07198 A (GENETICS INST) 27 February 1997 (1997-02-27) the whole document ---	
A	EP 0 834 563 A (SMITHKLINE BEECHAM CORP) 8 April 1998 (1998-04-08) the whole document ---	
P,X	EP 0 962 530 A (LILLY CO ELI) 8 December 1999 (1999-12-08) the whole document ---	1-16, 18-21
P,X	WO 00 21986 A (INCYTE PHARMA INC ;KLINGLER TOD M (US); VOLKMUTH WAYNE (US); WALKE) 20 April 2000 (2000-04-20) seq.ID.11 the whole document ---	1-14, 18-21
P,X	KIM, I. ET AL.: "Molecular cloning, expression, and characterization of angiopoietin-related protein. Angiopoietin-related protein induces endothelial cell sprouting." JOURNAL OF BIOLOGICAL CHEMISTRY, 10 September 1999 (1999-09-10), pages 26523-8, XP002146664 the whole document -----	1-16,20, 21

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/14042

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-21 all partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: claims 1-21, all partially

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0196 (seq.ID.4), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0196, chimeric protein comprising a portion corresponding to PR0196, antibody against siad protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto.

2. Claims: Inventions 2-24: claims 1-21, all partially,
and as far as applicable

Subject matter as defined for invention 1, but limited to the respective genes (nucleic acid/protein seq.ID's):

2. PR0444 (Seq.ID's 8 & 9),
3. PR0183 (Seq.ID's 10 & 11),
4. PR0185 (Seq.ID's 12 & 13),
5. PR0210 (Seq.ID's 14 & 15),
6. PR0215 (Seq.ID's 16 & 17),
7. PR0217 (Seq.ID's 21 & 22),
8. PR0242 (Seq.ID's 23 & 24),
9. PR0288 (Seq.ID's 28 & 29),
10. PR0365 (Seq.ID's 31 & 32),
11. PR01361 (Seq.ID's 38 & 39),
12. PR01308 (Seq.ID's 40 & 41),
13. PR01183 (Seq.ID's 51 & 52),
14. PR01272 (Seq.ID's 53 & 54),
15. PR01419 (Seq.ID's 55 & 56),
16. PR04999 (Seq.ID's 57 & 58),
17. PR07170 (Seq.ID's 62 & 63),
18. PR0248 (Seq.ID's 64 & 65),
19. PR0353 (Seq.ID's 72 & 73),
20. PR01318 (Seq.ID's 77 & 78),
21. PR01600 (Seq.ID's 79 & 80),
22. PR09940 (Seq.ID's 83 & 84),
23. PR0350 (Seq.ID's 131 & 132), and
24. PR06309 (Seq.ID's 138 & 139).

3. Claims: Invention 25: claims 1-39, all partially

Subject matter as defined for invention 1, but limited to PR0533 (seq.ID's 85 & 86). In addition, method for detecting PR0533 through use of its binding partner FGFR-4, and vice versa, use of said binding pair to link a bioactive molecule

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

to a cell presenting one of the binding partners using the counterpart which carries said molecule, and use of the binding partner to modulate the activity of the counterpart.

4. Claims: Inventions 26-38: claims 1-39, all partially, and as far as applicable

Subject matter as defined for invention 23, but limited to the respective genes (nucleic acid/protein seq.ID's):

- 26.PRO301 (Seq.ID's 90 & 91), which binds to itself,
- 27.PRO187 (Seq.ID's 98 & 99), which binds to FGFR-3, FGFR-1, FGFR-2, or FGFR-4,
- 28.PRO337 (Seq.ID's 103 & 104), which binds to PRO6004,
- 29.PRO1411 (Seq.ID's 107 & 108), which binds to PRO4356,
- 30.PRO10096 (Seq.ID's 125 & 126), which binds to PRO2630,
- 31.PRO246 (Seq.ID's 109 & 110), which binds to itself,
- 32.PRO6307 (Seq.ID's ?? & ??), which binds to PRO265,
- 33.PRO6003 (Seq.ID's 127 & 128), which binds to PRO941,
- 34.PRO6004 (Seq.ID's 129 & 130), which binds to PRO337,
- 35.PRO4356 (Seq.ID's 107 & 108), which binds to PRO1411,
- 36.PRO2630 (Seq.ID's 136 & 137), which binds to PRO10096,
- 37.PRO265 (Seq.ID's 114 & 115), which binds to PRO6307, and
- 38.PRO941 (Seq.ID's 53 & 54), which binds to PRO6003.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PLT/US 00/14042

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9915653	A	01-04-1999	US 5972338 A	26-10-1999
			US 6057435 A	02-05-2000
			AU 9388098 A	12-04-1999
			EP 1015585 A	05-07-2000

WO 9707198	A	27-02-1997	US 5707829 A	13-01-1998
			AU 6712396 A	18-02-1997
			AU 6768596 A	12-03-1997
			CA 2227220 A	06-02-1997
			CA 2229208 A	27-02-1997
			EP 0839196 A	06-05-1998
			EP 0851875 A	08-07-1998
			JP 11510045 T	07-09-1999
			US 6043344 A	28-03-2000
			WO 9704097 A	06-02-1997
			US 6074849 A	13-06-2000
			US 5969093 A	19-10-1999

EP 0834563	A	08-04-1998	JP 10179178 A	07-07-1998
			US 5824504 A	20-10-1998

EP 0962530	A	08-12-1999	AU 4320499 A	20-12-1999
			WO 9962925 A	09-12-1999

WO 0021986	A	20-04-2000	AU 6417799 A	01-05-2000
			EP 1037915 A	27-09-2000
